

In the Specification:

Please replace the paragraph beginning at page 13, line 2, with the following rewritten paragraph:

Figure 1 shows the nucleotide sequences of the coding regions of human ANT1 ("ANT1m") (SEQ ID NO: 1), human ANT2 ("ANT2m") (SEQ ID NO: 2) and human ANT3 ("ANT3m") (SEQ ID NO: 3).

Please replace the paragraph beginning at page 13, line 4, with the following rewritten paragraph:

Figure 2 shows the polypeptide sequences of human ANT1 ("ANT1p") (SEQ ID NO: 4), human ANT2 ("ANT2p") (SEQ ID NO: 5) and human ANT3 ("ANT3p") (SEQ ID NO: 6).

Please replace the paragraph beginning at page 19, line 25, with the following rewritten paragraph:

The compositions and methods of the present invention can be adapted to any prokaryotic or eukaryotic ANT, including plant and animal ANTs, which may further include, for example, yeast, vertebrate, mammalian, rodent, primate and human ANTs, for which amino acid sequences and/or encoding nucleic acids will be known to those familiar with the art. Three human ANT isoforms have been described that differ in their tissue expression patterns. (Stepien et al., 1992 *J. Biol. Chem.* 267:14592; *see also* Wallace et al., 1998 in *Mitochondria & Free Radicals in Neurodegenerative Diseases*, Beal, Howell and Bodis-Wollner, Eds., Wiley-Liss, New York, pp. 283-307, and references cited therein.) Nucleic acid sequences for cDNAs encoding these three human ANT isoforms have been reported (Figure 1; *See* Neckelmann et al., *Proc. Nat'l. Acad. Sci. U.S.A.* 84:7580-7584 (1987) for huANT1 cDNA [SEQ ID NO:1]; Battini et al., *J. Biol. Chem.* 262:4355-4359 (1987) for huANT2 cDNA [SEQ ID NO:2], and Cozens et al., *J. Mol. Biol.* 206:261-280 (1989) for huANT3 cDNA [SEQ ID NO:3]; *see* Figure 2 for amino acid sequences of

huANT1 [~~SEQ ID NO: 31~~] (SEQ ID NO: 4) huANT2 [~~SEQ ID NO: 32~~] (SEQ ID NO: 5) and huANT3 [~~SEQ ID NO: 33~~] (SEQ ID NO: 6), and ANT gene sequences have been determined for a number of species (See, *e.g.*, Li et al., 1989 *J. Biol. Chem.* 264:13998 for huANT1 genomic DNA, see also, *e.g.*, Li et al. 1990 *J. Biol. Chem.* 265:20585; Liew et al. GenBank Acc. #N86710 for huANT2; Shinohara et al., 1993 *Biochim. Biophys. Acta* 1152:192 for rat ANT gene; for others see also, *e.g.*, Ku et al., 1990 *J. Biol. Chem.* 265:16060; Adams et al., 1991 *Science* 252:1651; and WO 98/19714.). The present invention further relates to nucleic acids which hybridize to ANT encoding polynucleotide sequences as provided herein, as incorporated by reference or as will be readily apparent to those familiar with the art, if there is at least 70%, preferably at least 90%, and more preferably at least 95% identity between the sequences. The present invention particularly relates to nucleic acids which hybridize under stringent conditions to the ANT encoding nucleic acids referred to herein. As used herein, the term "stringent conditions" means hybridization will occur only if there is at least 95% and preferably at least 97% identity between the sequences. The nucleic acids which hybridize to ANT encoding nucleic acids referred to herein, in preferred embodiments, encode polypeptides which either retain substantially the same biological function or activity as the ANT polypeptides encoded by the cDNAs of Figure 1 [~~SEQ ID NOS: 1, 2 and 3~~], or the deposited expression constructs.

Please replace the paragraph beginning at page 21, line 27, with the following rewritten paragraph:

The nucleic acids which encode ANT polypeptides, for example the human ANT polypeptides having the amino acid sequences of Figure 2 [~~SEQ ID NOS: 31-33~~] (SEQ ID NOS: 4-6) or any other ANT polypeptides for use according to the invention, or for the ANT polypeptides encoded by the deposited constructs may include, but are not limited to: only the coding sequence for the ANT polypeptide; the coding sequence for the ANT polypeptide and additional coding sequence; the coding sequence for the ANT polypeptide (and optionally additional coding sequence) and non-coding sequence, such as introns or non-coding sequences 5' and/or 3' of the coding sequence for the ANT polypeptide, which for example may further include but need not be

limited to one or more regulatory nucleic acid sequences that may be a regulated or regulatable promoter, enhancer, other transcription regulatory sequence, repressor binding sequence, translation regulatory sequence or any other regulatory nucleic acid sequence. Thus, the term "nucleic acid encoding an ANT polypeptide" encompasses a nucleic acid which includes only coding sequence for the polypeptide as well as a nucleic acid which includes additional coding and/or non-coding sequence(s).

Please replace the paragraph beginning at page 22, line 12, with the following rewritten paragraph:

The present invention further relates to variants of the herein described nucleic acids which encode for fragments, analogs and derivatives of an ANT polypeptide, for example the human ANT1, ANT2 and ANT3 polypeptides having the deduced amino acid sequences of Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6) or any ANT polypeptide, including ANT polypeptides encoded by the cDNAs of the deposited expression constructs. The variants of the nucleic acids encoding ANTs may be naturally occurring allelic variants of the nucleic acids or non-naturally occurring variants. As is known in the art, an allelic variant is an alternate form of a nucleic acid sequence which may have at least one of a substitution, a deletion or an addition of one or more nucleotides, any of which does not substantially alter the function of the encoded ANT polypeptide. Thus, for example, the present invention includes nucleic acids encoding the same ANT polypeptides as shown in Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6), or the same ANT polypeptides encoded by the cDNAs of the deposited expression constructs, as well as variants of such nucleic acids, which variants encode a fragment, derivative or analog of any of the polypeptides of Figure 2 (SEQ ID NO:2) or the polypeptides encoded by the cDNAs of the deposited expression constructs.

Please replace the paragraph beginning at page 23, line 29, with the following rewritten paragraph:

The present invention further relates to ANT polypeptides, and in particular to methods for producing recombinant ANT polypeptides by culturing host cells containing ANT

expression constructs, and to isolated recombinant human ANT polypeptides, including, for example, the human ANT1, ANT2 and ANT3 polypeptides which have the deduced amino acid sequence of Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6) or which have the amino acid sequence encoded by the deposited recombinant expression constructs, as well as fragments, analogs and derivatives of such polypeptides. The polypeptides and nucleic acids of the present invention are preferably provided in an isolated form, and in certain preferred embodiments are purified to homogeneity.

Please replace the paragraph beginning at page 24, line 28, with the following rewritten paragraph:

The polypeptides of the present invention include ANT polypeptides and fusion proteins having amino acid sequences that are identical or similar to sequences known in the art. For example by way of illustration and not limitation, the human ANT ("huANT") polypeptides of Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6) are contemplated for use according to the instant invention, as are polypeptides having at least 70% similarity (preferably a 70% identity) to the polypeptides of Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6) and more preferably 90% similarity (more preferably a 90% identity) to the polypeptides of Figure 2 [~~SEQ ID NOS: 31-33~~] (SEQ ID NOS: 4-6) and still more preferably a 95% similarity (still more preferably a 95% identity) to the polypeptides of Figure 2 [~~SEQ ID NOS:31-33~~] (SEQ ID NOS: 4-6) and to portions of such polypeptides, wherein such portions of an ANT polypeptide generally contain at least 30 amino acids and more preferably at least 50 amino acids.

Please replace the paragraph beginning at page 59, line 25, with the following rewritten paragraph:

For human ANT1 (huANT1; SEQ ID NO:1), the following primers were used:
Forward (sense):

5'-TTATATCTCGAGTATGGGTGATCACGCTTGGAGCTTCCTAAAG ~~SEQ ID NO:4~~
(SEQ ID NO: 7)

and Reverse (antisense):

5'-TATATAGGTACCTTAGACATATTTTTTGATCTCATCATAACAAC ~~SEQ ID NO:5~~
(SEQ ID NO: 8).

Please replace the paragraph beginning at page 60, line 3, with the following rewritten paragraph:

For human ANT2 (huANT2; SEQ ID NO:2), the following primers were used:

Forward (sense):

5'-TTATATCTCGAGTATGACAGATGCCGCTGTGTCCTTCGCCAAG ~~SEQ ID NO:6~~
(SEQ ID NO: 9)

and Reverse (antisense):

5'-TATATAGGTACCTTATGTGTACTTCTTGATTTCATCATAAAG ~~SEQ ID NO:7~~
(SEQ ID NO: 10).

Please replace the paragraph beginning at page 60, line 18, with the following rewritten paragraph:

For rat ANT1 (rANT1), the following primers were used:

Forward (sense):

CTCGAGATGGGGGATCAGGCTTTGAGCT ~~SEQ ID NO:___~~
(SEQ ID NO: 11)

Reverse (antisense):

GGTACCTTACACATATTTTTTGATCTCATCATA ~~SEQ ID NO:___~~
(SEQ ID NO: 12)

Please replace the paragraph beginning at page 60, line 26, with the following rewritten paragraph:

For rat ANT2 (rANT2), the following primers were used:

Forward (sense):

CTCGAGATGACAGATGCCGCTGTGTCCT

~~SEQ ID NO: 13~~

(SEQ ID NO: 13)

Reverse (antisense):

GGTACCTTATGTGTACTTCTTGATTTCATCA

~~SEQ ID NO: 14~~

(SEQ ID NO: 14)

Please replace the paragraph beginning at page 62, line 1, with the following rewritten paragraph:

The recombinant huANT nucleotide sequences present in the expression constructs were determined and their authenticity confirmed relative to the published ANT sequences (Figure 1; See Neckelmann et al., *Proc. Nat'l. Acad. Sci. U.S.A.* 84:7580-7584 (1987) for huANT1 and Battini et al., *J. Biol. Chem.* 262:4355-4359 (1987) for huANT2 by sequencing using the PRISM™ Ready BIG DYE™ Terminator Cycle Sequencing Kit (The Perkin-Elmer Corp., Norwalk, CT) and the following sequencing primers 5'- TATGCCATAGCATTTTATCC (~~SEQ ID NO: 10~~) (SEQ ID NO: 15) and 5'- CGCCAAAACAGCCAAGCT (~~SEQ ID NO: 11~~) (SEQ ID NO: 16). For each human ANT sequence, both primers are located inside the vector sequence adjacent to the DNA insertion. Sequence data was analyzed using the SEQUENCE NAVIGATOR™ analysis software package (Perkin-Elmer).

Please replace the paragraph beginning at page 66, line 17, with the following rewritten paragraph:

A monospecific (anti-peptide) antibody that recognizes ANT1, ANT2 and ANT3 (hereinafter, a "Pan ANT antibody") was prepared as follows. A synthetic polypeptide corresponding to a portion of huANT3 located near the carboxy terminus and predicted to have high antigenicity according to the Jameson-Wolf Index (Wolf et al., *Comput. Appl. Biosci.* 4:187-191 (1988)) was synthesized using known means by Alpha Diagnostic International (San Antonio, TX) and determined to be at least about 70% pure, preferably at least about 90% pure, by HPLC and MS analyses. The sequence of the synthetic polypeptide (~~SEQ ID NO: 30~~) (SEQ ID NO: 17)

is:

Cys-Trp-Arg-Lys-Ile-Phe-Arg-Asp-Glu-Gly-Gly-Lys-Ala-Phe-Phe

Please replace the paragraph beginning at page 67, line 8, with the following rewritten paragraph:

A monospecific (antipeptide) antibody specific to ANT3 was prepared essentially according to the above-described procedure, with the exception that the synthetic peptide used was derived from a portion of the huANT3 polypeptide sequence, i.e., the following sequence (~~SEQ ID NO: —~~) (SEQ ID NO: 18):

Cys⁺-Ser-Gly-Thr-Glu-Arg-Glu-Phe-Arg-Gly-Leu-Gly-Asp-Cys-Leu-Val-Lys-Ile-Thr

The “Cys⁺” residue in this and the following immunogenic synthetic polypeptides refers to cysteine residues not present in the natural huANT3 polypeptide; these “extra” Cys residues were introduced to facilitate the linking of the peptide to KHL hemocyanin. Rabbits were inoculated with the KHL-peptide conjugate and bled essentially according to the above-described procedure.

Please replace the paragraph beginning at page 67, line 22, with the following rewritten paragraph:

A monospecific (antipeptide) antibody specific to ANT2 was prepared essentially according to the above-described procedure, with the exception that the synthetic peptide used had the following sequence (~~SEQ ID NO: —~~) (SEQ ID NO: 19) derived from huANT2:

Met-Thr-Asp-Ala-Ala-Val-Ser-Phe-Ala-Lys-Asp-Phe-Leu-Ala-Gly-Cys⁺

Please replace the paragraph beginning at page 68, line 2, with the following rewritten paragraph:

A monospecific (antipeptide) antibody specific to ANT1 was prepared essentially according to the above-described procedure, with the exception that the synthetic peptide used had

the following sequence (~~SEQ ID NO: 20~~) (SEQ ID NO: 20) derived from huANT1:

Met-Gly-Asp-His-Ala-Trp-Ser-Phe-Leu-Lys-Asp-Leu-Leu-Ala-Gly-Cys⁺

Please insert the enclosed "Sequence Listing" immediately after the section of the specification entitled "Abstract of the Disclosure" on page 118.